

and to 50mg in 3% of pts. The reasons for dose reduction were mainly rash 54%, diarrhea 19.4%, pruritus 9.7%; rash and diarrhea 6.5%.

Conclusions: Based on a large number of unselected pts with advanced NSCLC in Israel, the safety data obtained from the interim results with erlotinib confirm the favorable safety profile of erlotinib previously observed in clinical trials. To date, the results show erlotinib to be generally well tolerated, thus allowing most pts to receive the recommended daily dose of 150mg. Efficacy data may be available by September 2007.

P3-087 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

Phase II trial of sequenced bevacizumab and erlotinib with bevacizumab and chemotherapy for 1st line stage IIIB or IV Non-small cell lung cancer (NSCLC)

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Background: The addition of bevacizumab (B) to chemotherapy improves survival in patients (pts) with previously untreated metastatic NSCLC. The addition of bevacizumab to erlotinib (E) appears promising in second line therapy of NSCLC. Bevacizumab plus erlotinib (B+E) has never been tested in 1st line NSCLC.

Methods: Eligible pts with previously untreated stage IIIB (pleural effusion) or stage IV NSCLC and normal organ function without hemoptysis or brain metastasis were treated with B (15mg/kg every 21 days) plus E (150mg once daily) for 4 cycles (cycle- 21 days) followed by B (15mg/kg), carboplatin (AUC 6) and paclitaxel (200 mg/m²) every 21 days for 4 cycles. Pts who did not progress on initial B+E received maintenance therapy with B+E until progression.

Results: We have enrolled 40 pts (of 48 planned) in this ongoing study. The characteristics: 25 male, 15 female; median age 70 years; 37 stage IV, 3 stage IIIB; 3 never smokers; 26 adenocarcinoma, 10 non-small cell lung cancer not otherwise specified, 3 undifferentiated carcinoma, 1 adenocarcinoma with BAC; performance status 0 in 16 and 1 in 24. Twenty three pts have completed 4 cycles of B+E with 5 partial responses (22%), 13 stable disease (56%) and 5 progressive disease (22%). Sixteen pts have completed bevacizumab plus chemotherapy with best responses of 5 partial response (31%), 9 stable disease (56%), 2 progressive disease (12%). Of the 11 pts treated with maintenance B+E, 4 developed progressive disease and have discontinued therapy. The median number of cycles received during maintenance therapy with B+E was 6 (range 2-15+). Treatment related toxicities: related to B+E- grade 3 rash (3 pts), grade 3 fatigue (2 pts), and grade 3 epistaxis (1 pt); related to B and chemotherapy- grade 3 neuropathy (2 pts), grade 3 hypersensitivity reaction (1 pt), grade 4 neutropenia (2 pts), and grade 4 arterial thrombosis (1 pt). Most notably, there have been no major bleeding episodes so far.

Conclusions: 1. The combination of B+E achieved a disease control rate of 78% in previously untreated patients with IIIB/IV NSCLC and is well tolerated. 2. The initial administration of 4 cycles of B+E does not impair the efficacy platinum based doublet chemotherapy with bevacizumab.

P3-088 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

Serum E-cadherin does not associate with response to gefitinib in patients with non-small cell lung cancer (NSCLC)

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Background: The epidermal growth factor receptor (EGFR) is expressed in many human epithelial malignancies, including NSCLC. The response rates to EGFR tyrosine kinase inhibitors (TKIs) in unselected NSCLC patients ranges from 9-27%. NSCLC cell lines highly sensitive to EGFR TKIs express E-cadherin. Patients with high E-cadherin expression in tumors samples have improved time-to-progression (TTP) after treatment with EGFR TKI erlotinib, indicating the significant role of epithelial-mesenchymal transition (EMT) to predict sensitivity/resistance to EGFR inhibitors. These results suggest that high E-cadherin expression would be a clinically relevant biomarker for patient's selection to EGFR TKI therapy. The aim of the present study was to investigate the potential association between serum E-cadherin expression and clinical activity of gefitinib in European NSCLC patients.

Methods and Results: Serum E-cadherin levels were evaluated by ELISA using commercially available kit (R&D Systems). Statistical evaluation was performed by Kaplan-Meier analysis and a Cox proportional hazard model. Among 135 consecutive patients treated with gefitinib (median age, 67 years; 75% males; 83% ever smokers), 123 were evaluable for response, TTP and overall survival (OS). Forty-four (36%) had stable disease (SD) and 15 (13%) had objective response (OR). Serum E-cadherin levels ranged from 15 to 203 ng/mL with a median value of 30 ng/mL. The whole population was divided into two groups based on median E-cadherin levels (< 30 versus ≥ 30 ng/mL). Higher serum E-cadherin level was observed in patients with older age (P=.003), ECOG PS of 2 versus 0 or 1 (P=.027), and squamous cell histology (P=.045).

The response rates were 13% and 11% in patients with low and high E-cadherin level, respectively (P=.809); disease control rates were 52% and 44% respectively (P=.415). Median TTP and OS were 3.5 and 5.8 months, and 3 and 7 months, in patients with low and high E-cadherin levels (P=.245; P=.434 respectively).

Conclusions: These results indicate that higher E-cadherin levels are associated with age, advanced PS and squamous cell histology. Serum E-cadherin does not appear to predict response, TTP, and OS in patients with NSCLC after therapy with gefitinib. Corresponding E-cadherin tissue studies are ongoing.

P3-089 NSCLC: Molecular Targeted Therapy Posters, Wed, Sept 5 – Thurs, Sept 6

Gefitinib (G) treatment outcome after progression on erlotinib (E) in patients with advanced non-small-cell lung cancer (NSCLC)

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Background: Two case reports describe a response to E after failure of G (Garfield DH, J Clin Oncol 2005) or to G after failure of E (Choong NW et al, Nat Clin Pract Oncol 2006) in patients (pts) with advanced NSCLC. Otherwise, a limited experience in 5 pts suggests that E is not